

What is claimed:

1. An oligonucleotide which, during or after administration into the alimentary canal, has enhanced bioavailability compared to a phosphorothioate oligodeoxynucleotide of substantially the same sequence, wherein said oligonucleotide comprises at least one heteroatomic backbone modification and a 2'-alkoxyalkoxy modification.

2. (Cancelled).

3. (Cancelled).

4. (Cancelled).

5. (Cancelled).

6. (Cancelled).

7. (Cancelled).

8. The oligonucleotide of claim 1 wherein said 2'-alkoxyalkoxy modification is a 2'-methoxyethoxy modification.

9. (Cancelled).

1. 10. A pharmaceutical composition comprising the oligonucleotide of claim
11. The pharmaceutical composition of claim 10 which comprises a colloidal dispersion system.
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R2 12. The pharmaceutical composition of claim 10 which comprises at least one penetration enhancer.
13. The pharmaceutical composition of claim 12 wherein the penetration enhancer comprises a bile salt or a fatty acid.
14. The pharmaceutical composition of claim 13 wherein the bile salt is CDCA.
15. The pharmaceutical composition of claim 13 wherein the fatty acid is sodium caprate or sodium laurate.
16. The pharmaceutical composition of claim 13 which comprises both one or more bile salts and one or more fatty acids.
17. A pharmaceutical composition comprising an oligonucleotide having at least one 2'-alkoxyalkoxy modification and at least one 5-methylcytidine.
18. The pharmaceutical composition of claim 17 wherein said 2'-alkoxyalkoxy modification is a 2'-methoxyethoxy modification.
19. (Cancelled).

20. (Cancelled).

21. (Cancelled).

22. (Cancelled).

23. (Cancelled).

24. (Cancelled).

25. (Cancelled).

26. (Cancelled).

27. A method of modulating expression of a target nucleic acid comprising administering into the alimentary canal an effective amount of an oligonucleotide that has at least one nitrogenous heteroatomic backbone modification, hybridizes to said target nucleic acid, and modulates the expression thereof.

28. The method of claim 27 wherein said administration into the alimentary canal is oral, rectal, endoscopic, sublingual or buccal administration.

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29. The method of claim 27 wherein said heteroatomic backbone modification is a methylene(methylimino) modification.

30. The method of claim 27 wherein said administration into the alimentary canal is oral, rectal, endoscopic, sublingual or buccal administration.

31. The method of claim 27 wherein said oligonucleotide has a 2'-O-alkyl or 2'-alkoxyalkoxy modification.

32. The method of claim 31 wherein said 2'-O-alkyl modification is a 2'-O-methyl or 2'-O-propyl modification.

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33. The method of claim 31 wherein said 2'-alkoxyalkoxy modification is a 2'-methoxyethoxy modification.

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